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Journal Reviews

Gregg W. Stone, Akiko Maehara, Bernhard Witzenbichler, Jacek Godlewski, Helen Parise, Jan-Henk E. Dambrink, Andrzej Ochala, Trevor W. Carlton, Ecaterina Cristea, Steven D. Wolff, Sorin J. Brener, Saqib Chowdhary, Magdi El-Omar, Thomas Neunteufl, D. Christopher Metzger, Theodore Karwoski, Jose M. Dizon, Roxana Mehran, C. Michael Gibson, for the INFUSE-AMI Investigators, Intracoronary abciximab and aspiration thrombectomy in patients with large anterior myocardial infarction: the INFUSE-AMI randomized trial. JAMA 307 (17) (2012) 1817–1826

1. Context

Thrombus embolization during percutaneous coronary intervention (PCI) in ST-segment elevation myocardial infarction (STEMI) is common and results in suboptimal myocardial perfusion and increased infarct size. Two strategies proposed to reduce distal embolization and improve outcomes after primary PCI are bolus intracoronary abciximab and manual aspiration thrombectomy.

2. Objective

To determine whether bolus intracoronary abciximab, manual aspiration thrombectomy, or both reduce infarct size in high-risk patients with STEMI.

3. Design, setting, and patients

Between November 28, 2009, and December 2, 2011, 452 patients presenting at 37 sites in 6 countries within 4 h of STEMI due to proximal or mid left anterior descending artery occlusion undergoing primary PCI with bivalirudin anticoagulation were randomized in an open-label, 2×2 factorial design to bolus intracoronary abciximab delivered locally at the infarct lesion site vs no abciximab and to manual aspiration thrombectomy vs no thrombectomy.

4. Interventions

A 0.25 mg/kg bolus of abciximab was administered at the site of the infarct lesion via a local drug delivery catheter. Manual aspiration thrombectomy was performed with a 6 F aspiration catheter.

5. Main outcome measures

Primary end point: infarct size (percentage of total left ventricular mass) at 30 days assessed by cardiac magnetic resonance imaging (cMRI) in the abciximab vs no abciximab groups (pooled across the aspiration randomization); major secondary end point: 30-day infarct size in the aspiration vs no aspiration groups (pooled across the abciximab randomization).

6. Results

Evaluable cMRI results at 30 days were present in 181 and 172 patients randomized to intracoronary abciximab vs no abciximab, respectively, and in 174 and 179 patients randomized to manual aspiration vs. no aspiration, respectively. Patients randomized to intracoronary abciximab compared with no abciximab had a significant reduction in 30-day infarct size (median, 15.1%; interquartile range [IQR], 6.8%–22.7%; $n = 181$, vs. 17.9% [IQR, 10.3%–25.4%]; $n = 172$; $p = 0.03$). Patients randomized to intracoronary abciximab also had a significant reduction in absolute infarct mass (median, 18.7 g [IQR, 7.4–31.3 g]; $n = 184$, vs. 24.0 g [IQR, 12.1–34.2 g]; $n = 175$; $p = 0.03$) but not abnormal wall motion score (median, 7.0 [IQR, 2.0–10.0]; $n = 188$, vs. 8.0 [IQR, 3.0–10.0]; $n = 184$; $p = 0.08$). Patients randomized to aspiration thrombectomy vs no aspiration had no significant difference in infarct size at 30 days (median, 17.0% [IQR, 9.0%–22.8%]; $n = 174$, vs. 17.3% [IQR, 7.1%–25.5%]; $n = 179$; $p = 0.51$), absolute infarct mass (median, 20.3 g [IQR, 9.7–31.7 g]; $n = 178$, vs. 21.0 g [IQR, 9.1–34.1 g]; $n = 181$; $p = 0.36$), or abnormal wall motion score (median, 7.5 [IQR, 2.0–10.0]; $n = 186$, vs. 7.5 [IQR, 2.0–10.0]; $n = 186$; $p = 0.89$).

7. Conclusion

In patients with large anterior STEMI presenting early after symptom onset and undergoing primary PCI with bivalirudin anticoagulation, infarct size at 30 days was significantly reduced by bolus intracoronary abciximab delivered to the infarct lesion site but not by manual aspiration thrombectomy.

8. Perspective

In this multicenter, prospective, randomized trial in patients with large anterior STEMI presenting early after infarct onset and undergoing primary PCI with bivalirudin anticoagulation, the principal findings were: 1) bolus intracoronary abciximab delivered to the site of the lesion via a clearway catheter significantly but modestly reduced the infarct size at 30 days 2) thrombus aspiration with export catheter had no effect on infarct size and 3) indices of myocardial reperfusion, ST

resolution (STR) and 30-day MACE (~7% in all groups)/stent thrombosis/bleeding were not significantly different between the randomized groups.

Two of the strongest baseline determinants of infarct size are: 1) anterior MI location and 2) abnormal TIMI flow. This trial was limited to patients with proximal or mid LAD occlusion and TIMI 0–2 flow. Moreover, it only enrolled patients who could be treated early, in whom time window for effective myocardial salvage had not closed. The median time from symptom onset to hospital arrival was only 99 min and the median D-to-B time was 45 min. Thus the study population represents a highly selected cohort of patients with large anterior MI, in whom infarct size reduction should be feasible given early presentation and rapid treatment. Infarct size was assessed by cMRI, which strongly correlates with subsequent mortality. Unlike prior studies, which measured infarct size at 2–7 days (a period during which substantial myocardial edema is present, thereby interfering with assessment of viable myocardium) in this study cMRI was done at 30 days when much of myocardial edema had resolved.

These results need to be placed in the context of previous studies. A meta-analysis of 6 RCT's (1246 patients) reported enhanced survival with bolus intracoronary abciximab. However, the recent AIDA-STEMI trial (2065 patients) found nearly identical rates of MACE with bolus intracoronary and intravenous abciximab. However, this trial differs from these earlier studies in many ways: 1) unlike prior studies which included routine post-PCI intravenous abciximab infusion in both the groups, in this trial **only bolus intracoronary abciximab** was given in the randomized groups. 2) In all prior trials (including AIDA-STEMI), intracoronary abciximab was infused proximally through the guide catheter thereby limiting its penetration into occlusive thrombus and allowing spillage of the drug to LCx or backflow into the aorta. In contrast, the local drug delivery catheter **(clearway catheter)** used in this study achieves high intra-clot concentration of abciximab at the site of LAD occlusion and prolongs drug residence time, which may enhance platelet disaggregation and thrombus resolution. In the present study, an abciximab bolus delivered directly to the infarct lesion site (without a 12-hour infusion) reduced infarct size at 30 days in patients with anterior STEMI reperfused early.

Regarding aspiration thrombectomy, in TAPAS, 1071 patients with anterior and non-anterior STEMI who presented within 12 h of symptoms at a single-center were randomized to manual aspiration vs. no aspiration before primary PCI; aspiration resulted in modest improvements in MBG and STR but a marked reduction in 1-year mortality. Other trials have reported conflicting results, and in contrast to single-center studies, multicenter aspiration trials have been largely negative. Moreover, in TAPAS, aspiration did not reduce infarct size as measured by cardiac biomarkers, calling into question the mechanism underlying the survival benefit. The present multicenter trial, in which only patients presenting early with anterior MI and coronary anatomy optimal for aspiration were enrolled, and in which cMRI was used to assess infarct size at 30 days was specifically designed to overcome many of the limitations from these earlier studies. The fact that manual thrombus aspiration did not reduce infarct size in this study makes a substantial clinical benefit unlikely, questioning its routine use in STEMI.

9. Our opinion

Regarding use of GPIIb/IIIa inhibitors: a) I/V bolus and infusion is to be discouraged because it achieves very little intra-clot concentration and also increases the risk of systemic bleeding. b) Only bolus intracoronary drug should be used, that too not into the guide catheter, but via a clearway catheter (we can use a simple PTCA balloon by making multiple holes on its surface, in case clearway catheter is not available).

Regarding manual aspiration via Export catheter: a) the symptom onset to hospital arrival and the D-to-B time were substantially shorter in this study which is next to impossible in our context. b) As time passes by after STEMI thrombus tends to get organized and hence thrombus aspiration might have some role to play in late presenters of STEMI. However, the last word in this matter is yet to be written.

Suraj Khanal*
Assistant Professor of Cardiology, Department of Cardiology, 3rd Floor, Block-C, Advanced Cardiac Center, PGIMER, Chandigarh 160012, India

Ajay Bahl
Associate Professor of Cardiology, PGIMER, Chandigarh, India

*Corresponding author. Tel.: +91 09878222526.
E-mail address: khanal.s@rediffmail.com

Azeem Latib, Antonio Colombo, Fausto Castriota, Antonio Micari, Alberto Cremonesi, Francesco De Felice, Alfredo Marchese, Maurizio Tespili, Patrizia Presbitero, Gregory A. Sgueglia, Francesca Buffoli, Corrado Tamburino, Ferdinando Varbella, Alberto Menozzi, A randomized multicentre study comparing a paclitaxel drug-eluting balloon with a paclitaxel-eluting stent in small coronary vessels: The BELLO (Balloon Elution and Late Loss Optimization) study. J Am Coll Cardiol. 60 (2012) 2473–2480

Objectives: The aim of this study was to evaluate the efficacy of drug-eluting balloons (DEB) compared with paclitaxel eluting stents (PES) for the reduction of restenosis in small vessels.

Background: DEB have been shown to be effective in the treatment of coronary in-stent restenosis, but data are limited regarding their efficacy in de-novo disease.

Methods: BELLO (Balloon Elution and Late Loss Optimization) is a prospective, multicentre trial that randomized 182 patients with lesions located in small vessels (reference diameter <2.8 mm) to treatment with paclitaxel DEB and provisional bare-metal stenting ($n = 90$) or PES implantation ($n = 92$). The primary endpoint was noninferiority of angiographic in-stent (in-balloon) late loss with a delta of 0.25 mm. Secondary endpoints were angiographic restenosis, target lesion revascularization, and major adverse cardiac events (MACE; death, myocardial infarction, target vessel revascularization) at 6 months.

Results: Baseline characteristics were well matched, except for a smaller vessel size in the DEB group